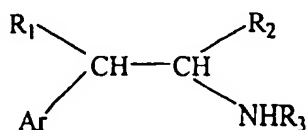


**We claim:**

- I. A method comprising the steps of:
- identifying a subject with a depressive disorder; and
  - administering an effective amount of a composition comprising a carbonic anhydrase activator and a pharmaceutically acceptable carrier to said subject, wherein the activator is selected from the group consisting of:

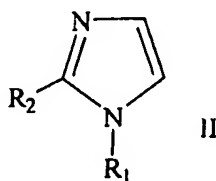
(1) structure I



I (I)

wherein R<sub>1</sub> is H or OH; R<sub>2</sub> and R<sub>3</sub> are independent H, COOH or lower alkyl, for example linear, branched or cyclic C<sub>1</sub>-C<sub>6</sub> alkyl or C<sub>1</sub>-C<sub>4</sub> alkyl; and Ar is phenyl, imidazolyl or phenyl or imidazolyl substituted with one or more halo, hydroxy, amino or lower alkyl groups for example linear, branched or cyclic C<sub>1</sub>-C<sub>6</sub> group or C<sub>1</sub>-C<sub>4</sub> alkyl group;

(2) structure II:

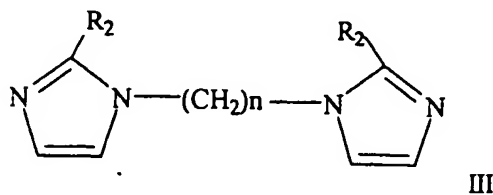


II

(II)

wherein R<sub>1</sub> and R<sub>2</sub> are independently H or lower alkyl, for example linear, branched or cyclic C<sub>1</sub>-C<sub>6</sub> alkyl or C<sub>1</sub>-C<sub>4</sub> alkyl;

(3) structure III:



III

(III)

wherein  $n$  is 1 or 2 and  $R_2$  is H or lower alkyl, for example linear, branched or cyclic  $C_1$ - $C_6$  alkyl or  $C_1$ - $C_4$  alkyl; and  
pharmaceutically acceptable salts of I, II, or III.

2. The method of claim 1, wherein the activator has structure I wherein  $R_1$  is H or OH;  $R_2$  is H,  $CH_3$  or  $COOH$ ;  $R_3$  is H or  $CH_3$ ; and Ar is phenyl, or a substituted phenyl.
3. The method of claim 2, wherein the substituted phenyl is 4-hydroxyphenyl, 4-fluorophenyl, 4-aminophenyl, 3-amino-4-hydroxyphenyl, or 3,4-dihydroxyphenyl.
4. The method of claim 1, wherein the activator has structure I wherein  $R_1$  is H or OH;  $R_2$  is H,  $CH_3$  or  $COOH$ ;  $R_3$  is H or  $CH_3$ ; and Ar is imidazole or a substituted imidazole.
5. The method of claim 4, wherein the substituted imidazole is imadazol-4-yl-, or 5-methylimidazole-4-yl-.
6. The method of claim 1, wherein the activator has structure II wherein  $R_1$  is H, methyl, ethyl or propyl; and  $R_2$  is H or methyl.
7. The method of claim 1, wherein the activator is structure III wherein  $n$  is 1 or 2; and  $R^2$  is H or methyl.
8. The method of claim 1, wherein the activator is selected from the group consisting of: imidazole, phenylalanine, a substituted ethylamine, phenethylamine, histamine, histidine, a linked di-imidazole, a triazole, and pharmaceutically acceptable salts thereof.
9. The method of claim 8, wherein the activator is histidine.
10. The method of claim 8, wherein the activator is histamine.
11. The method of claim 8, wherein the activator is phenylalanine.
12. The method of claim 8, wherein the activator is 4-hydroxy phenylalanine.
13. The method of claim 8, wherein the activator is 4-fluoro phenylalanine.
14. The method of claim 8, wherein the activator is 3, 4-dihydroxy phenylalanine.

15. The method of claim 8, wherein the activator is 3-amino-4-hydroxyphenylalanine.
16. The method of claim 8, wherein the activator is 4-amino phenylalanine.
17. The method of claim 8, wherein the activator is tyrosine.
18. The method of claim 8, wherein the activator is dopamine.
19. The method of claim 8, wherein the activator is noradrenaline.
20. The method of claim 8, wherein the activator is adrenaline.
21. The method of claim 8, wherein the activator is histamine.
22. The method of claim 8, wherein the activator is 5-methyl histamine.
23. A method of treating depression in a subject in need thereof, comprising administering an effective amount of a composition comprising a carbonic anhydrase activator and a pharmaceutically acceptable carrier, wherein the activator is selected from the group consisting of: an aromatic amine or an aromatic amino acid wherein the aromatic amine or aromatic amino acid contains a single aromatic group.
24. The method of claim 23, wherein the activator is selected from the group consisting of: phenylalanine, a substituted phenylalanine, histidine, a substituted histidine, a substituted phenylalanineimidazole, a substituted imidazole, a linked di-imidazole, and a linked substituted di-imidazole.
25. The method of claim 1, wherein the activator is an aromatic amine or an aromatic amino acid wherein the aromatic amine or aromatic amino acid contains a single aromatic group.
26. The method of claim 25, wherein the aromatic amine is selected from the group consisting of dopamine, noradrenaline, adrenaline, histamine, and 5-methyl histamine.
27. The method of claim 23, wherein the aromatic amine is selected from the group consisting of dopamine, noradrenaline, adrenaline, histamine, and 5-methyl histamine.

28. The method of claim 1, wherein the activator activates intraneuronal carbonic anhydrase.
29. A method comprising the steps of:
- a) identifying a subject with a depressive disorder; and
  - b) administering an effective amount of a composition comprising a protein kinase C activator and a pharmaceutically acceptable carrier to said subject, wherein the PKC activator is selected from a group consisting of: FGF-18, a macrocyclic lactone, a benzolactam, a pyrrolidinone, or a combination thereof.
30. The method of claim 29, wherein the macrocyclic lactone is a bryostatin or neristatin.
31. The method of claim 30, wherein the bryostatin is selected from a group consisting of bryostatin-1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 and 18.
32. The method of claim 31, wherein the bryostatin is bryostatin-1.
33. The method of claim 30, wherein the neristatin is neristatin-1.
34. A method of treating depression in a subject in need thereof, comprising administering an effective amount of a composition comprising a protein kinase C activator and a pharmaceutically acceptable carrier, wherein the activator is selected from the group consisting of: FGF-18, a macrocyclic lactone, a benzolactam, a pyrrolidinone, or a combination thereof.
35. The method of claim 34, wherein the macrocyclic lactone is a bryostatin or neristatin.
36. The method of claim 35, wherein the bryostatin is selected from a group consisting of bryostatin-1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 and 18.
37. The method of claim 36, wherein the bryostatin is bryostatin-1.
38. The method of claim 35, wherein the neristatin is neristatin-1.
39. A method for screening an agent for antidepressant activity, comprising the steps of:

- a) administering an agent in a pharmaceutically acceptable carrier to a test subject and administering the pharmaceutically acceptable carrier to the control subject;
  - b) individually placing said test and control subject into a pool of water and measuring the distance and/or duration of swimming during a testing period; and
  - c) comparing the distance or duration of swimming of the test subject to a control subject, wherein increased distance or duration of swimming of the test subject compared to the control subject is indicative of antidepressant activity.
40. The method of claim 39, wherein the pool is round.
41. The method of claim 40, wherein the pool has a diameter of between 100 and 200 cm.
42. The method of claim 41, wherein the pool has a diameter of 150 cm.
43. The method of claim 39, wherein the pool provides no escape.
44. The method of claim 39, wherein steps (a), (b), and (c) are repeated.
45. The method of claim 44, wherein the steps are repeated three times.
46. The method of claim 39, wherein the distance and/or duration of swimming is measured by video means.